

71. The composition of claim 70, wherein the ITR cassette is within an HSV vector.

72. The composition of claim 69, further comprising a second HSV that comprises an ITR cassette.

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cont
73. A recombinant herpes simplex virus (HSV) comprising a rep gene, which comprises a promoter operatively linked to a polynucleotide encoding an adeno-associated virus (AAV) rep polypeptide, wherein the rep polypeptide or the promoter is conditionally active, and wherein the promoter is an inducible promoter.

74. A recombinant herpes simplex virus (HSV) comprising a rep gene, which comprises a promoter operatively linked to a polynucleotide encoding an adeno-associated virus (AAV) rep polypeptide, wherein the rep polypeptide is active at a first permissive temperature, and inactive at a second nonpermissive temperature.

IN THE SPECIFICATION:

Please amend the paragraph at page 3, lines 8-20, of the specification to read as follows:

B2
U.S. Patent 5,856,152 describes a hybrid adenovirus-AAV vector including an ITR cassette within an adenovirus genome. While the system is apparently able to produce high-titer AAV stocks, it suffers from a number of drawbacks chiefly attributed to the properties of adenoviruses. For example, adenoviruses can be manipulated to carry only up to about 7.5 kb of exogenous DNA. Thus, where the rep and cap genes are introduced into the adenoviral genome, the carrying capacity of the ITR cassette is diminished. Deleting certain genes from the adenoviral genome can increase the carrying capacity of the vector; however, such gene products must be supplied *in trans* either to support adenoviral growth or to provide sufficient helper function to produce the desired AAV vector. Of course, such steps require either novel cell lines or secondary transfections to supply the deleted adenoviral genes, manipulations that tend to reduce AAV titer, as described above.

Please amend the paragraph at page 4, line 36, through page 5, line 14, to read as follows:

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While the HSV for use in the present invention is not an amplicon-based system, it can contain one or more mutations in HSV genes. Indeed, it is preferred that the vectors contain mutations in one or more genes essential for HSV replication so that such vectors are constrained to replicate as HSV viruses only in permissive cells. Any such mutation can be introduced into the HSV genome, many of which are known in the art (see, e.g., DeLuca, *et al.*, *J. Virol.*, 56, 558-70

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cont (1985), Samaniego *et al.*, *J. Virol.* 69(9), 5705-15 (1996); Field *et al.*, *J. Hygiene*, 81, 267-77 (1978); Cameron *et al.*, *J. Gen. Virol.*, 69, 2607-12 (1988); Fink *et al.*, *Hum. Gene Ther.*, 3, 11-19, (1992); Jamieson *et al.*, *J. Gen. Virol.*, 76, 1417-31 (1995); Chou *et al.*, *Science*, 250, 1262-66 (1990); Sears *et al.*, *J. Virol.*, 55, 338-46 (1985), U.S. Patents 5,658,724 and 5,804,413, and International Patent Application WO 98/15637). Such mutations can, for example, affect one or a combination of immediate early, early, or late genes. Desirably, the HSV backbone contains deficiencies in one or more essential genes to reduce toxicity within packaging and host cells (see, e.g., U.S. Patents 5,879,934, 5,804,413, and 5,658,724, all to DeLuca).

Please amend the paragraph at page 7, line 29, through page 8, line 13, of the specification to read as follows:

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Through the use of the inventive HSV, the invention provides a method of directing site-specific integration of an AAV-derived ITR cassette into a desired target DNA molecule, such as a chromosome within a host cell. In accordance with this method, the ITR cassette and the inventive HSV are introduced into the host cell. Expression of the rep gene(s) within the cell so as to deliver the active encoded rep protein(s) within the cell can effect excision of the ITR from the vector and, desirably, integration of the ITR cassette within the desired target DNA molecule. Of course, where the ITR is introduced into the cell within a larger polynucleotide vector (e.g., an extrachromosomal polynucleotide such as a plasmid or virus), the method further effects excision of the cassette from the vector. By virtue of the aforementioned inactivation of essential HSV genes, the method can facilitate the safe delivery of AAV-derived ITR cassettes for use in populations of host cells, which can be *in vivo* or *in vitro*. For example, the method can be employed to deliver genes to isolated CD34⁺ lymphocytes *in vitro* which can then be employed in immunological protocols. An exemplary *in vivo* application could involve efficient delivery of active genes (e.g., encoding cytokines, a suicide gene, or other bioactive compound with antitumor activity) to dividing cells within a tumor. Additionally, where such host cells are mitotically-active, the ITR cassette (having integrated into the chromosomal DNA) will be retained by successive generations of mitotic offspring, whereas the HSV backbone will not, by virtue of its inability to replicate in the absence of the essential HSV genes.